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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/591,465

06/29/2007

Pascal Perriat

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EXAMINER

DO, PENSEE T

ART UNIT

PAPER NUMBER

1641

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DELIVERY MODE

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/591,465	Applicant(s) PERRIAT ET AL.	
	Examiner Pensee T. Do	Art Unit 1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 27 October 2010.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-30 is/are pending in the application.
- 4a) Of the above claim(s) 25-30 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-24 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☒ Claim(s) 1-30 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Priority

This application 10591465, **PG Pub. No. 20070281324** filed 06/29/2007 is a national stage entry of PCT/FR05/00491 , International Filing Date: 03/02/2005 and claims foreign priority to 0402115 , filed 03/02/2004. The effective filing date is 3/2/2004.

Amendment Entry & Claims Status

The amendment filed on October 27, 2010 has been acknowledged and entered.

Claims 1-30 are pending.

Claims 25-30 are withdrawn.

Claims 1-24 are being examined.

Claim Objections

Claim 16 is objected to because of the following informalities: claim 16 recites "Np" twice. Appropriate correction is required.

Withdrawn Rejection(s)

Rejection under 112, 2nd paragraph in the previous office action is withdrawn herein.

Maintained Rejection(s)

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory

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obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-4, 7-15, 18-22, 24 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-12, 14-16, 19-22, 24 and 31 of copending Application No. 12/293,486 (***copending appl. '486***) in view of Li et al (US 2004/0075083).

Copending appl. '486 claims nanoparticles comprising a core and shell structure, wherein the core is made up of rare earth metal oxide such as europium and a coating of thickness between 1-10 nm.

However, copending appl. '486 fails to teach a polysiloxane coating and at least one biological ligand grafted by covalent bonding to the polysiloxane coating.

Li teaches Europium (Eu)-containing fluorescent nanoparticles comprising an aluminum oxide framework having Europium activator, and at least one energy reservoir selected from Mg, Ca, Sr and Ba and one co-activator such as Sc, Y, La, Ce, Pr, Nd, etc...(see [0006]). The nanoparticles are coated with a silicon-containing compound such as siloxane or polysiloxane which contains functional groups through which biological molecules such as proteins, nucleic acids, carbohydrate are bound (see [0036], [0026]).

Therefore, it would have been obvious to one of ordinary skill in the art to coat the nanoparticle copending appl. '486 with a functionalized polysiloxane coating as taught by Li so that the nanoparticles of copending appl. '486 can be used as labels in biological assays. One of ordinary skill in the art would have a reasonable expectation of success when combining the teachings of Li and copending appl. '486 because both teach using nanoparticles that are doped with rare earth elements such as Europium.

This is a provisional obviousness-type double patenting rejection.

Claims 5 and 6 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-12, 14-16, 19-

22, 24 and 31 of copending Application No. 12/293,486 (***copending appl. '486***) in view of Li et al (US 2004/0075083) as applied to claim 1 above, and further in view of Yates et al. (US 4,921,589).

Copending appl. '486 and Li have been discussed above.

However, they fail to teach covalently attaching 100 to 1000 molecules of organic fluorescent molecules to the coating of the nanoparticles and such organic fluorescent molecules are fluorescein or rhodamine.

Yates teaches applying a coating of polysiloxanes onto a substrate such as spheres or glass spheres (see col. 7, lines 10-22); Then applying a solution of photosensitizers such as fluorescein or rhodamine onto the polysiloxane coating. (see col. 4, line 50-col. 5, lines 13). Yates teaches the coating of polysiloxane of formula I, II or III on col. 5, line 43-col. 6, line 39) with m or n being integers of 200-2000 which represents how many molecules of siloxanes in the polysiloxane. Thus, when the photosensitizers are coated onto the polysiloxane, they would bind through the O-Si bond or C-Si bond of the polysiloxane (see col. 5, lines 13-16) and thus since there are 200-2000 siloxanes or O-Si or C-Si bonds are available, 200-2000 of organic fluorescent molecules would bind. The photosensitizer produces singlet oxygen which has a long enough lifetime to be chemically active in solution. The singlet oxygen is also a stronger oxidizing agent (see col. 1, lines 5-17).

Thus, one of ordinary skill in the art would have been covalently attach Rhodamine or Fluorescein onto polysiloxane coating of the nanoparticles in copending appl. '486 modified with Li by the method taught by Yates since these photosensitizers

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produce singlet oxygen which is a stronger oxidizing agent. One of ordinary skill in the art would have a reasonable expectation of success in combining these teachings since they all teach using polysiloxane coating on spheres.

This is a provisional obviousness-type double patenting rejection.

Claim 16 is provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-12, 14-16, 19-22, 24 and 31 of copending Application No. 12/293,486 (***copending appl. '486***) in view of Li et al (US 2004/0075083) as applied to claim 1 above, and further in view of O'Beirne (US 7,101,719 filed on Nov. 5, 2001).

Copending appl. '486 and Li have been discussed above.

However, they fail to teach 0.01% to 50 % of the metal cations of the nanosphere are uranide cations chosen from Ac, Th, Pa, Np, U, Pu.

O'Beirne teaches doping an inorganic host material such as yttrium oxide (see col. 6, lines 1-15) with an activator such as uranium. (see col. 6, lines 14-30).

Since it is well known in the art uranium can be used as an activator for doping inorganic host material such as yttrium oxide beside terbium, europium, erbium, etc, it would have been obvious to one of ordinary skill in the art to add uranium to yttrium oxide of copending appl. '486 modified with Li to obtain nanoparticles doped with rare earth metal cations such as uranium to produce a nanoparticle with a unique emission spectrum distinguished from the other nanoparticles doped with a different activator. One of ordinary skill in the art would have a reasonable expectation of success in

combining these teachings since they all teach doping nanoparticles with rare earth metal cations.

This is a provisional obviousness-type double patenting rejection.

Claims 17 is provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-12, 14-16, 19-22, 24 and 31 of copending Application No. 12/293,486 (***copending appl. '486***) in view of Li et al (US 2004/0075083) as applied to claim 1 above, and further in view of Kresse et al. (US 5,427,767).

Copending appl. '486 and Li have been discussed above.

However, they fail to teach adding U^{235} or Gd^{157} .

Kresse teaches that: "Another possible approach to therapy can be taken by insertion of **[Fe]** into ferrites and accomplishing neutron activation for thermal and epithermal neutrons taking advantage of the large capture cross section of **[Fe]**. As in resonant nuclear absorption through photons (Mossbauer) described above, tissue containing no **[Fe]** will scarcely take up neutrons and consequently will not be detrimentally affected. Neutron uptake is primarily concentrated on the areas containing **[Fe]**. Hence, sufficient enrichment of the tumor provided, radiation damage is inflicted only on the tumor by secondary radiation (Auger electrons and photons). The **[Fe]** must be doped with the appropriate isotopes for application of ferrite/magnetite in therapy. (see col. 5, lines 34-45).

Since Kresse teaches doping magnetic nanoparticles with ^{157}Gd for application in cancer therapy, it would have been obvious to ordinary skill in the art to incorporate Gd^{157} as an activator or dopant into the magnetic host of copending appl. '486 modified with Li to obtain nanoparticles doped with Gd^{157} for use in cancer therapy. One of ordinary skill in the art would have a reasonable expectation of success in combining these teachings because they all teach using Gd as a dopant in magnetic hosts, i.e. Y_2O_3 .

This is a provisional obviousness-type double patenting rejection.

Claim 23 is provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-12, 14-16, 19-22, 24 and 31 of copending Application No. 12/293,486 (***copending appl. '486***) in view of Li et al (US 2004/0075083) as applied to claim 1 above, and further in view of Molina et al. (Chem. Mater. 2001, 13, 2818-2823).

Copending appl. '486 and Li have been discussed above.

However, they fail to teach a water-soluble polymer such as dextran or polyethylene glycol is grafted onto the coating of the nanoparticle.

Molina teaches mixing polyethylene glycol with siloxane to coat Eu^{3+} and such coating offers high visible transparency, flexibility and good chemical stability. When these materials contain Europium ions, potentially interesting phosphors are obtained. The nature of the Eu^{3+} first coordination shell in these hybrids of polyethylene and

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siloxane may be tuned, as a function of both the salt concentration and the polymer molecular weight. (see entire document especially pg. 2818, col. 2).

Thus, it would have been obvious to one of ordinary skill in the art to combine polyethylene glycol and siloxane or polysiloxane as the coating to coat Eu³⁺ to obtain nanoparticles with a shell of high visible transparency, flexibility and good chemical stability (see Molina p. 2818, col.2) as taught by Molina. One of ordinary skills in the art would have a reasonable expectation of success in combining the teachings of Molina with copending appl. '486 modified with Li since they all teach using nanoparticles doped with Europium ions.

This is a provisional obviousness-type double patenting rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-4, 7-15, 18-22, 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bazzi et al. (Journal of Luminescence 102-103 (2003) p. 445-450 submitted by applicants) in view of Li et al. (US 2004/0075083) and Baumann et al. (US 6,099,964).

Bazzi teaches a highly luminescent hybrid nanoparticle comprising a nanosphere of diameter from 2-5 nm (see abstract), of which at least 90% by weight consists of sesquioxides Ln_2O_3 and doped Ln^{3+} yttrium or gadolinium oxides ($\text{Ln}=\text{Eu}, \text{Tb}, \text{Nd}, \text{Gd}$, or Y) (which are rare earth elements) (see entire document especially p. 446, col. 2, 1st paragraph and p. 450).

However, Bazzi fails to teach that the nanoparticle has a polysiloxane coating having a mean thickness within the range from 0.5 to 10 nm; and at least one biological ligand grafted by covalent bonding to the polysiloxane coating.

Li teaches Europium (Eu)-containing fluorescent nanoparticles comprising an aluminum oxide framework having Europium activator, and at least one energy reservoir selected from Mg, Ca, Sr and Ba and one co-activator such as Sc, Y, La, Ce, Pr, Nd, etc...(see [0006]). The nanoparticles are coated with a silicon-containing compound such as siloxane or polysiloxane which contains functional groups through which biological molecules such as proteins, nucleic acids, carbohydrate are bound (see [0036], [0026]).

Therefore, it would have been obvious to one of ordinary skill in the art to coat the nanoparticle of Bazzi with a functionalized polysiloxane coating as taught by Li so that the nanoparticles of Bazzi can be used as labels in biological assays. One of ordinary skill in the art would have a reasonable expectation of success when combining the teachings of Li and Bazzi because both teach using nanoparticles that are doped with rare earth elements such as Europium.

However, Bazzi and Li fail to teach the polysiloxane layer has a thickness between 0.5 to 10 nm.

Baumann et al. teach organopolysiloxane particles which have an average diameter of 5-200 nm. The particles have a siloxane shell with a thickness of 1 to 100 nm. (see abstract; col. 5, lines 18-19).

Since it is well known in the art that polysiloxane coating with a thickness of 1-100 nm are used to obtain particles with average size of 5-200 nm as taught by Baumann, it would have been obvious to one of ordinary skill in the art to coat the particles of Bazzi and Li with a thickness of 2-100 nm to obtain particles size of 5-200 nm in order to completely cover the core. One of ordinary skill in the art would have a reasonable expectation of success in combining the teachings of Bazzi, Li and Baumann since they all teach obtaining nanoparticles with average size of 5 nm.

For claim 2, since Li teaches the same polysiloxane coating as that of the present invention, 5 to 75 % of the silicon atoms must be bound to four other silicon atoms by oxygen bridges in such polysiloxane taught by Li.

For claims 3 and 4, since Li teaches the same polysiloxane coating as that of the present invention, such polysiloxane coating in Li must have a density of 1.6 to 2.4 or less than 2.

For claim 7, Bazzi teaches that the nanoparticles contain at least 80% by weight of a rare earth sesquioxides (see entire document especially p. 446, col. 2, 1st paragraph and p. 450).

For claims 8 and 9, Bazzi teaches that the nanosphere, for at least 80% by weight, consists of Gd_2O_3 or Y_2O_3 . (see entire document especially p. 446, col. 2, 1st paragraph and p. 450).

For claim 10, Bazzi teaches the nanosphere is doped with a lanthanide of type Eu, Tb, Er, Nd, Yb representing from 0.1 to 25% of the metal cations. (see entire document especially p. 446, col. 2, 1st paragraph and p. 450; pp. 447 results and discussion).

For claims 11, 12, 14 and 15, Bazzi teaches that the nanosphere is doped with a lanthanide of type Nd or Yb, or Er. (see entire document especially p. 446, col. 2, 1st paragraph and p. 450; pp. 447 results discussion).

For claim 13, Bazzi teaches the nanosphere is doped with at least two different lanthanides representing from 0.1 to 25% of the metal cations, at least one of these is Eu, i.e. $Y_2O_3:Eu$ (see entire document especially p. 446, col. 2, 1st paragraph and p. 450; pp. 447 results discussion).

For claim 18, Li teaches coating the nanoparticle with polyclonal antibody. (see [0056]).

For claim 19, Li teaches that the coating composition of the nanoparticle has one or more functional groups and these functional groups are used to link biological molecules onto the particles. (see [0036]). Thus, it would have been obvious to one of ordinary skill in the art that those nanoparticles which are coated with a coating having two functional groups would be bound to two different biological molecules.

For claim 20, Li teaches the grafted biological ligand is a carbohydrate. (see [039]).

For claim 21, Li teaches the nanoparticles are bound to small molecules (complexing molecules) other than biological molecules. (see [0036]).

For claim 22, Li teaches phosphate (organophosphate) or DNA, RNA (also an organophosphate) is grafted onto the coating. (see [0036]).

For claim 24, Bazzi teaches the colloidal suspension of the hybrid nanoparticles. (see p. 446, col. 2, first paragraph).

Claims 5, 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bazzi in view of Li and Baumann as applied to claim 1 above, and further in view of Yates et al. (US 4,921,589).

Bazzi, Li and Baumann have been discussed above.

However, they fail to teach covalently attaching 100 to 1000 molecules of organic fluorescent molecules to the coating of the nanoparticles and such organic fluorescent molecules are fluorescein or rhodamine.

Yates teaches applying a coating of polysiloxanes onto a substrate such as spheres or glass spheres (see col. 7, lines 10-22); Then applying a solution of photosensitizers such as fluorescein or rhodamine onto the polysiloxane coating. (see col. 4, line 50-col. 5, lines 13). Yates teaches the coating of polysiloxane of formula I, II or III on col. 5, line 43-col. 6, line 39) with m or n being integers of 200-2000 which represents how many molecules of siloxanes in the polysiloxane. Thus, when the

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photosensitizers are coated onto the polysiloxane, they would bind through the O-Si bond or C-Si bond of the polysiloxane (see col. 5, lines 13-16) and thus since there are 200-2000 siloxanes or O-Si or C-Si bonds are available, 200-2000 of organic fluorescent molecules would bind. The photosensitizer produces singlet oxygen which has a long enough lifetime to be chemically active in solution. The singlet oxygen is also a stronger oxidizing agent (see col. 1, lines 5-17).

Thus, one of ordinary skill in the art would have been covalently attach Rhodamine or Fluorescein onto polysiloxane coating of the nanoparticles in Bazzi modified with Li and Baumann by the method taught by Yates since these photosensitizers produce singlet oxygen which is a stronger oxidizing agent. One of ordinary skill in the art would have a reasonable expectation of success in combining these teachings since they all teach using polysiloxane coating on spheres.

Claim 16 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bazzi in view of Li and Baumann as applied to claim 1 above, and further in view of O'Beirne (US 7,101,719 filed on Nov. 5, 2001).

Bazzi, Li and Baumann have been discussed above.

However, they fail to teach 0.01% to 50 % of the metal cations of the nanosphere are uranide cations chosen from Ac, Th, Pa, Np, U, Pu.

O'Beirne teaches doping an inorganic host material such as yttrium oxide (see col. 6, lines 1-15) with an activator such as uranium. (see col. 6, lines 14-30).

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Since it is well known in the art uranium can be used as an activator for doping inorganic host material such as yttrium oxide beside terbium, europium, erbium, etc, it would have been obvious to one of ordinary skill in the art to add uranium to yttrium oxide of Bazzi and modified with Li and Baumann to obtain nanoparticles doped with rare earth metal cations such as uranium to produce a nanoparticle with a unique emission spectrum distinguished from the other nanoparticles doped with a different activator. One of ordinary skill in the art would have a reasonable expectation of success in combining these teachings since they all teach doping nanoparticles with rare earth metal cations.


Claim 17 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bazzi in view of Li and Baumann as applied to claim 1 above, and further in view of Kresse et al. (US 5,427,767).

Bazzi, Li and Baumann have been discussed above.

However, they fail to teach adding U^{235} or Gd^{157} .

Kresse teaches that: "Another possible approach to therapy can be taken by insertion of ^{157}Gd into ferrites and accomplishing neutron activation for thermal and epithermal neutrons taking advantage of the large capture cross section of ^{157}Gd . As in resonant nuclear absorption through photons (Mossbauer) described above, tissue containing no ^{157}Gd will scarcely take up neutrons and consequently will not be detrimentally affected. Neutron uptake is primarily concentrated on the areas containing ^{157}Gd . Hence, sufficient enrichment of the tumor provided,

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radiation damage is inflicted only on the tumor by secondary radiation (Auger electrons and photons). The  must be doped with the appropriate isotopes for application of ferrite/magnetite in therapy. (see col. 5, lines 34-45).

Since Kresse teaches doping magnetic nanoparticles with ^{157}Gd for application in cancer therapy, it would have been obvious to ordinary skill in the art to incorporate Gd^{157} as an activator or dopant into the magnetic host of Bazzi modified with Li and Baumann to obtain nanoparticles doped with Gd^{157} for use in cancer therapy. One of ordinary skill in the art would have a reasonable expectation of success in combining these teachings because they all teach using Gd as a dopant in magnetic hosts, i.e. Y_2O_3 .

Claim 23 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bazzi in view of Li and Baumann as applied to claim 1 above, and further in view of Molina et al. (Chem. Mater. 2001, 13, 2818-2823).

Bazzi, Li and Baumann have been discussed above.

However, they fail to teach a water-soluble polymer such as dextran or polyethylene glycol is grafted onto the coating of the nanoparticle.

Molina teaches mixing polyethylene glycol with siloxane to coat Eu^{3+} and such coating offers high visible transparency, flexibility and good chemical stability. When these materials contain Europium ions, potentially interesting phosphors are obtained. The nature of the Eu^{3+} first coordination shell in these hybrids of polyethylene and

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siloxane may be tuned, as a function of both the salt concentration and the polymer molecular weight. (see entire document especially pg. 2818, col. 2).

Thus, it would have been obvious to one of ordinary skill in the art to combine polyethylene glycol and siloxane or polysiloxane as the coating to coat Eu³⁺ to obtain nanoparticles with a shell of high visible transparency, flexibility and good chemical stability (see Molina p. 2818, col.2) as taught by Molina. One of ordinary skills in the art would have a reasonable expectation of success in combining the teachings of Molina with Bazzi modified with Li and Baumann since they all teach using nanoparticles doped with Europium ions.

Response to Arguments

Applicant's arguments filed October 27, 2010 have been fully considered but they are not persuasive.

Regarding the double patenting rejection, applicants submit that the rejection is improper since the applied application is prior art against the instant application. Further, it is not co-owned by the Assignee of this application so that a Terminal Disclaimer could be properly filed.

This is not found persuasive because:

The applied application is NOT prior art against the present application sine the applied application 12/293,486 has an effective filing date of March 20, 2006 which is after the effective filing date of the instant application which is March 2, 2004.

Therefore, the OPD rejection is properly maintained.

Regarding all the 103 rejections by Bazzi in view of Li and further in view of Baumann, Applicants argue that the Li and Baumann references are not combinable with the Bazzi reference because:

1/. In Li, the size and composition of the nanoparticles are different from the composition of the nanospheres in Bazzi. Li teaches the nanoparticle core having an aluminum oxide framework with a Europium activator and at least one co-activator selected from the group consisting of yttrium and certain lanthanide elements. The nanoparticles are coated with a siloxane or polysiloxane having reactive functional groups for attachment of the nanoparticles to a desired biological or chemical target molecule. In contrast, the core of Bazzi is made up of sesquioxides Ln_2O_3 and doped Ln^{3+} yttrium and gadolinium oxides ($\text{Ln} = \text{Eu}$ (europium), Tb, Nd, Gd or Y which are rare earth elements).

This is not found persuasive because:

Li teaches coating a core doped with Europium and yttrium or certain lanthanide elements with a polysiloxane coating. The similarity between the core of Bazzi and the core of Li is that they both have a core composition doped with Europium and yttrium.

2/. Applicants further submit that the coating in the present invention must increase the size of the obtained nanoparticles and that the composition surface of the nanosphere modifies the physic-chemical conditions of the sol-gel technique used for coating. Furthermore, Applicants argue that the method of obtaining the coating in Li is different from the method of obtaining the coating in the present invention, i.e. heat use

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vs. no heat use, and that the coating in the present invention is not only for protective purpose but for IRM applications as well.

This is not found persuasive because:

Regarding the intended use of the coating, i.e. the coating must not increase the overall size of the nanoparticles, mentioned by Applicants above, since this limitation is not found anywhere in claim 1, it is irrelevant and no further discussion is necessary.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., the coating must not increase the overall particle size) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Regarding the method of obtaining the coating, i.e. heat use vs. no heat use, this is irrelevant to the recited claims which are drawn to a composition. Therefore, no further discussion is necessary.

Regarding the intended use of the coating, i.e. IRM applications or MRI applications, this is also irrelevant because:

In response to applicant's argument that using the coating for IRM applications, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim.

3/. Regarding the Baumann reference, Applicants argue that Baumann does not remedy the failings in the rejection based on Li. First, the particles describes in Baumann are even more removed from the nanoparticles of the claimed invention than the particles of Li. Baumann does not describe the combination of a nanosphere, of mean diameter included in the range from 2-9 nm with a coating around the nanosphere having a mean thickness range of 0.5 - 10 nm which corresponds to a thick coating compared to the dimension of the core. Applicants conclude that the Examiner merely just plucked the thickness of the coating in Baumann to use in the rejection, while ignoring the fact that siloxane shell of Baumann is produced in a context which is completely and totally unrelated to either Bazzi or Li.

This is not found persuasive because:

Baumann is relied upon for the teaching of a polysiloxane coating thickness. Since Li teaches that polysiloxane shell can be used to coat a core doped with rare earth elements such as Ytrrium or Europium, and Baumann teaches using polysiloxane at a certain thickness to coat core comprising of metal atoms and the nanoparticles in Baumann has a size range of 5-200 nm which overlaps the claimed range of nanoparticles in the present invention (2-9nm), it would have been obvious to one of ordinary skill in the art to coat the polysiloxane in Li on the nanoparticle core of Bazzi with a thickness taught by Baumann. Baumann is related to Li and Bazzi for using a polysiloxane to coat a core comprising of metal atoms and that such coating is used to coat nanoparticles which are 5 nm in size.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pensee T. Do whose telephone number is 571-272-0819. The examiner can normally be reached on Monday-Friday, 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya can be reached on 571-272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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/Pensee T. Do/
Examiner, Art Unit 1641
/Jacob Cheu/
Primary Examiner, Art Unit 1641